Pregnancy and child outcome after assisted reproduction techniques

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The introduction and widespread application of assisted reproduction techniques have raised major concern about the outcome of resulting pregnancies, as well as about the offspring’s health. It seems that pregnancies achieved after standard in-vitro fertilization (IVF) bear an increased risk for prematurity and low birth weight. On the other hand, pregnancy outcome of singletons achieved after intracytoplasmic sperm injection (ICSI) and after the transfer of frozen-thawed embryos is similar to that of spontaneously conceived singletons, and pregnancy complications are related only to gestation multiplicity. The incidence of congenital and chromosomal anomalies after standard IVF seems to be similar to that expected in the general population. The prevalence of congenital malformations does not seem to be higher after ICSI. On the other hand, there is a slightly increased risk for transmission of chromosomal aberrations of paternal origin and a higher risk of de novo, mainly sex-chromosomal aberrations. Postnatal growth and development of children born after standard IVF and cryopreservation seem to be within the normal ranges. Growth of ICSI children is also normal while their mental development needs further investigation. Family functioning in assisted reproduction families is better.

Key words: child development/chromosomal anomalies/congenital malformations/family functioning/pregnancy outcome

Introduction

The significant advances in the field of human reproduction and the introduction of various assisted reproduction techniques to alleviate infertility have raised major concerns about the health of the offspring, since several stages of natural fertilization are usually bypassed while early embryonic development takes place in vitro. Moreover, apart from the potential risk for genetic defects, malformations and other adverse consequences for the children born after assisted reproduction
Table I. Prospective evaluation of singleton pregnancy outcome after standard in-vitro fertilization (IVF) compared with natural conceptions in groups of mothers matched for age, parity, inclusion date and hospital of delivery.

<table>
<thead>
<tr>
<th></th>
<th>Preterm deliveries</th>
<th>Low birth weight Babies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard IVF (%)</td>
<td>8.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>13.4&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Spontaneous (%)</td>
<td>3.05&lt;sup&gt;b&lt;/sup&gt;</td>
<td>7.3&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> versus <sup>b</sup>: P < 0.05. <sup>c</sup>Total number of pregnancies in each group not available. Adapted from de Mouzon et al. (1998).

Techniques, another interesting question is whether there is any association between the type of conception and the obstetric or perinatal outcome.

The topic has become even more complicated since each technique may bear a different risk for the children and, theoretically, the more aggressive the technique, the higher the possible risk. Furthermore, the wide application of assisted conception all over the world and the increased number of pregnancies achieved by these means reinforce the urgent need for valid data on the health of children born after these procedures.

**Obstetric and perinatal outcome**

**In-vitro fertilization (IVF)**

Several studies have shown that the incidence of preterm deliveries and of low birth weight babies is higher in pregnancies achieved after IVF than in natural conceptions. Although this is mainly due to the higher frequency of multiple births after IVF, it seems that singleton IVF pregnancies also bear an increased risk for prematurity and, to a lesser extent, for low birth weight babies compared with the spontaneously conceived singletons.

Initially, several investigators described an increased incidence of preterm deliveries and low birth weight babies for singleton IVF pregnancies compared with the general population but with no adjustment for maternal background characteristics (Lancaster, 1985; Beral and Doyle, 1990; Rizk et al., 1991; Wennerholm et al., 1991; Doyle et al., 1992; de Mouzon et al., 1993; Tanbo et al., 1995). Therefore, the absence of a properly selected control group represents a serious limitation to these studies. However, the differences for singleton IVF pregnancies exist even when they are compared prospectively with a properly selected control group of natural conceptions matched on maternal age and parity (Tan et al., 1992; Wang et al., 1994; von During et al., 1995) as well as on inclusion date and hospital of delivery (de Mouzon et al., 1998) (Table I).

Several investigators have reported a higher incidence of pregnancy-induced hypertension and bleeding during pregnancy due to placenta praevia in singletons after IVF (Wennerholm et al., 1991; Doyle et al., 1992; Tanbo et al., 1995),
Pregnancy and child outcome after assisted reproduction techniques

Table II. Pregnancy outcome of singletons after intracytoplasmic sperm injection (ICSI)

<table>
<thead>
<tr>
<th></th>
<th>ICSI</th>
<th>General population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnanies (n)</td>
<td>140</td>
<td>9753</td>
</tr>
<tr>
<td>Mean gestational age (weeks)</td>
<td>39.9</td>
<td>39.4</td>
</tr>
<tr>
<td>≤37 weeks (%)</td>
<td>9.3</td>
<td>7.3</td>
</tr>
<tr>
<td>Mean birthweight (%)</td>
<td>3470</td>
<td>3417</td>
</tr>
<tr>
<td>≤2500 g (%)</td>
<td>6.4</td>
<td>6.1</td>
</tr>
</tbody>
</table>

Adapted from Wennerholm et al. (1996)

Table III. Pregnancy outcome of multifetal pregnancies after intracytoplasmic sperm injection (ICSI)

<table>
<thead>
<tr>
<th></th>
<th>Singleton</th>
<th>Twins</th>
<th>Triplets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children (n)</td>
<td>465</td>
<td>379</td>
<td>33</td>
</tr>
<tr>
<td>Mean birthweight (g)</td>
<td>3197</td>
<td>2436</td>
<td>1574</td>
</tr>
<tr>
<td>≤37 weeks (%)</td>
<td>11</td>
<td>53</td>
<td>100</td>
</tr>
<tr>
<td>≤2500 g (%)</td>
<td>10</td>
<td>39</td>
<td>94</td>
</tr>
<tr>
<td>≤1500 g (%)</td>
<td>2</td>
<td>4</td>
<td>55</td>
</tr>
</tbody>
</table>

Adapted from Bonduelle et al. (1996).

although in the French in-vitro national study, the frequency of pre-eclampsia and placenta praevia was comparable to the general population (FIVNAT, 1995).

It seems that these increased risks for singleton IVF pregnancies are associated with patient’s characteristics, such as increased maternal age and lower previous parity (Doyle et al., 1992) but the underlying cause of infertility and ovarian stimulation may also play a significant role (de Mouzon et al., 1998).

Intracytoplasmic sperm injection (ICSI)

The successful application of ICSI in the management of severe oligoastheno-teratozoospermia or even azospermia stimulated interest in the obstetric and perinatal outcome of the pregnancies achieved by this novel technique. The incidence of preterm deliveries for singletons after ICSI seems to be very close to that observed either in the general population (Table II), (Wennerholm et al., 1996; Wisanto et al., 1996) or in a control group matched for maternal age and parity (Wennerholm et al., 1996). Moreover, mean birthweight for singletons is similar after ICSI and after natural conception (Wennerholm et al., 1996; Wisanto et al., 1996).

On the other hand, the frequency of pregnancy-induced hypertension and bleeding complications seem to be higher among singletons after ICSI compared to the general population (Wennerholm et al., 1996). This is probably due to the increased rate of primiparity and multiplicity of these gestations (Wennerholm et al., 1996). Similarly, prematurity and low birthweight after ICSI are also related to pregnancy multiplicity (Bonduelle et al., 1996; Wennerholm et al., 1997) (Table III). There is no evidence, however, that the use of epididymal or
B.C. Tarlatzis and G. Grimbizis

Table IV. Pregnancy outcome of singletons after intracytoplasmic sperm injection (ICSI) according to the origin of the spermatozoa

<table>
<thead>
<tr>
<th></th>
<th>Ejaculate</th>
<th>Epididymal</th>
<th>Testicular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancies (n)</td>
<td>419</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>Mean (±SD) birthweight (kg)</td>
<td>3.2 ± 0.6</td>
<td>3.5 ± 0.5</td>
<td>3.5 ± 0.6</td>
</tr>
<tr>
<td>≤37 weeks (n)</td>
<td>49 (11.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages. Adapted from Wisanto et al. (1996).

testicular spermatozoa for ICSI yielded a higher obstetric risk for the pregnancies as compared to the use of ejaculated spermatozoa (Wisanto et al., 1996), (Table IV).

It seems that the obstetric outcome is similar in pregnancies after ICSI and after natural conception. A possible explanation is that the majority of patients treated by ICSI have only male factor infertility, whilst the female partner is healthy and without any pelvic pathology (Wennerholm et al., 1997).

**Oocyte donation**

Oocyte donation is now used widely in women with ovarian failure, usually of advanced age, and more rarely in patients with functional ovaries but carrying genetic diseases. Women who become pregnant after oocyte donation, especially those with ovarian failure, were found to have a higher risk for first trimester uterine bleeding, pregnancy-related hypertension and intrauterine growth retardation (Pados et al., 1994). Although these complications are more frequent in older women (>35 years), they are also observed in younger ones achieving a pregnancy with oocyte donation.

Most of these problems are manageable but women who became pregnant after oocyte donation should be followed closely in centres well equipped for high risk pregnancies. On the other hand, oocyte donation in extremely old women (>50 years) should be avoided.

**Embryo freezing**

Cryopreservation and subsequent transfer of frozen-thawed embryos may confer considerable benefits by increasing the number of pregnancies in an assisted reproduction techniques program. However, an adverse effect of the freeze-thaw process on pregnancy outcome cannot be excluded. Sutcliffe et al. (1995) found that the mean birth weight and mean gestational age at delivery were lower in pregnancies after transfer of frozen-thawed embryos than in naturally conceived pregnancies matched by maternal age and social class but not for multiplicity. These differences could be explained by the higher incidence of multiple gestations in the frozen-thawed group (Sutcliffe et al., 1995).

On the other hand, Wennerholm et al. (1997), in a cohort of 270 children (163 singletons, 98 individuals from twin pregnancies and nine individuals from triplet
Pregnancy and child outcome after assisted reproduction techniques

Table V. Pregnancy outcome of singletons after standard in-vitro fertilization (IVF) and cryopreservation of embryos.

<table>
<thead>
<tr>
<th></th>
<th>Standard IVF</th>
<th>Cryopreservation</th>
<th>Spontaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancies (n)</td>
<td>160</td>
<td>163</td>
<td>160</td>
</tr>
<tr>
<td>≤37 weeks (%)</td>
<td>11.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.6</td>
<td>5.6&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>≤2500 g (%)</td>
<td>7.5</td>
<td>5.0</td>
<td>4.7</td>
</tr>
</tbody>
</table>

<sup>a</sup> versus <sup>b</sup>; P < 0.05. Adapted from Wennerholm et al. (1997).

Table VI. ESHRE survey on intracytoplasmic sperm injection (ICSI): malformations in children conceived after the transfer of fresh and frozen/thawed ICSI embryos (until 31 December 1995)

<table>
<thead>
<tr>
<th></th>
<th>Ejaculated</th>
<th>Epididymal</th>
<th>Testicular</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fresh</td>
<td>Frozen</td>
<td>Fresh</td>
</tr>
<tr>
<td>Children born</td>
<td>2486</td>
<td>139</td>
<td>119</td>
</tr>
<tr>
<td>Malformations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>47 (1.9)</td>
<td>3 (2.2)</td>
<td>0</td>
</tr>
<tr>
<td>Minor</td>
<td>185 (7.4)</td>
<td>13 (9.3)</td>
<td>3 (2.5)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages. Adapted from Tarlatzis and Bili (1998).

pregnancies) conceived after transfer of frozen-thawed embryos, found that in singletons the mean birth weight, gestational age at delivery and APGAR score were similar to naturally conceived babies (Table V). Furthermore, Testart (1998) recently reported that babies born after 15 567 frozen-thawed embryo transfers had a higher mean birth weight and a lower incidence of embryo hypotrophy than babies born after 93 015 fresh transfers (Testart, 1998).

It appears, therefore, that the cryopreservation process itself has no impact on gestation outcome, and that, from the time of implantation, pregnancies induced with frozen-thawed embryos are no longer at a disadvantage compared with those occurring either spontaneously (Wennerholm et al., 1997) or after IVF with fresh embryos (Testart, 1998).

Congenital malformations and chromosomal aberrations

In-vitro fertilization

The incidence of congenital and chromosomal abnormalities after standard IVF seems to be between 2.0 and 2.5% in large assisted reproduction surveys (Beral and Doyle, 1990; Friedler et al., 1992; ASRM/SART, 1995; Bachelot and Thepot, 1995; de Mouzon and Lancaster, 1995, 1997; Lancaster et al., 1995) and is similar to that expected in the general population. It should be noted, however, that in surveys of assisted reproduction offspring, the follow-up is usually more detailed and hence anomalies that would not necessarily be detected in the general population might be identified. Moreover, the age of IVF parents is usually higher and the incidence of multiples is also increased compared with
the general population, which may also adversely influence the malformation rate. Thus, the normal congenital and chromosomal anomaly rates, despite these potential biases, are quite reassuring even in the absence of a proper control group.

**Intracytoplasmic sperm injection**

The introduction of assisted fertilization, initially by subzonal insemination (SUZI) and, subsequently, by ICSI raised new concerns about the health of the offspring. ICSI is indeed a more invasive technique since one spermatozoon is injected through the oocyte membrane directly into the cytoplasm, and fertilization can be achieved from spermatozoa that could never previously have been used in fertility treatment. Thus, fertilization can be obtained from ejaculated spermatozoa in cases of extremely severe oligoasthenoteratozoospermia but also from epidydimal and testicular spermatozoa in cases of azoospermia.

Several factors may lead to an additional risk because of the ICSI procedure: (i) selective mechanisms against physiologically or genetically abnormal spermatozoa might be bypassed, (ii) abnormal oocytes might be fertilized, (iii) the altered environment or the mechanical and chemical damage to the oocyte might lead to perturbations of meiosis and mitosis, and (iv) various chemical or environmental exposures might lead to point mutations, resulting in genetic diseases visible at birth (Bonduelle et al., 1996). The safety of this novel technique should therefore be assessed carefully.

**Congenital malformations**

The incidence of major congenital malformations in a cohort of 877 children born after ICSI and followed up prospectively at the Dutch speaking Free University of Brussels until July 1995 was found to be 2.6% (Bonduelle et al., 1996). This was later confirmed in a larger cohort of 1987 children where the incidence was 2.3% (Bonduelle et al., 1998a), as well as by the ESHRE Task Force on ICSI where the incidence after ICSI with ejaculated spermatozoa was found to be between 1.9–2.2% (Tarlatzis, 1996; Tarlatzis and Bili, 1998), (Table IV). This prevalence of major malformations is comparable to the rate observed in children born after natural conception (Lechat and Dolk, 1993) and is therefore reassuring. A major malformation in these studies was defined as any anomaly leading to functional impairment or necessitating surgical correction while the remaining ones were considered as minor.

However, Kurinczuk and Bower (1997) tried to recalculate the incidence of major congenital anomalies in the first study of the Belgian group (Bonduelle et al., 1996) using a different classification system; birth defects were defined according to the British Paediatric Association’s ICD-9 system (British Paediatric Association, 1979) and the type (minor or major) according to a method derived from the Centres for the Disease Control in the USA (Bower and Stanley, 1983). Thus, they calculated that the incidence of major anomalies in this group was 7.38% (confidence interval 1.99 to 5.55%) which was significantly higher than
Pregnancy and child outcome after assisted reproduction techniques

in the Australian general population where the incidence is 3.78%. Nevertheless, a recalculation of the major malformations even with these definitions by the Belgian group revealed an incidence not higher than 5.23% (Bonduelle et al., 1997). Furthermore, an overestimation due to the more detailed assessment and the longer period of follow-up of the children born after ICSI should also be taken into account.

It appears, therefore, that patients can be reassured on the basis of the available data, although there is a need for large prospective studies with well designed control groups on the basis of a common approach for detecting birth defects and using the same, widely accepted definitions (Kurinczuk and Bower, 1997; Bonduelle et al., 1998a).

Chromosomal aberrations

The incidence of chromosomal abnormalities after ICSI is an important issue concerning the safety of this technique. In’t Veld et al. (1995) opened the discussion on this question by reporting an extremely high incidence of de novo sex-chromosomal abnormalities in a small number of prenatal diagnostic tests performed for reasons of high maternal age (five out of 15 or 33.3%). However, the same investigators later reported a significantly lower risk in a greater number of prenatal tests (nine out of 71 or 12.7%) (Van Opstal et al., 1997). Most of them were of paternal (six out of nine) or maternal origin (two out of nine), (Van Opstal et al., 1997), but this incidence still seems to be extremely high even though it is derived from a small selected cohort of pregnancies.

On the other hand, Bonduelle et al. (1998a) reported the results from 1082 prenatal tests (690 amniocenteses and 392 chorionic villus samplings) performed in an unselected population of pregnancies achieved after ICSI, in which the indication for prenatal diagnosis was the ICSI procedure itself. There were 28 (2.6%) abnormal tests; 10 of them (0.92%) were inherited (one of them unbalanced) chromosomal abnormalities while the remaining 18 (1.66%) were de novo chromosomal aberrations (nine sex-chromosomal and nine autosomal). The father was the carrier in all but one case of the inherited chromosomal anomalies, indicating that this higher risk is predictable for the individual couples and not for the procedure itself.

Nevertheless, the incidence of sex-chromosomal de novo aberrations observed by Bonduelle et al. (1998a) (0.83%, 95% confidence interval 0.3–1.6%) is significantly higher than that observed in the general population (0.19–0.23%) (Nielsen and Wohlert, 1991; Jacobs et al., 1992). Similarly, there is also an increase in the risk of autosomal aberrations; although trisomies could be due partly to the increased maternal age, the incidence of structural de novo aberrations (four out of 1082 or 0.36%) is significantly higher than that recorded in the literature (0.07%) (Jacobs et al., 1992). The increased risk for these de novo chromosomal abnormalities may result from the ICSI procedure itself or may be linked to a subgroup of males with impaired semen samples (Bonduelle et al., 1998a). However, although all de novo sex-chromosomal aberrations were found
B.C. Tarlatzis and G. Grimbizis

in cases of extreme oligoasthenoteratozoospermia, no relationship has so far been observed between their occurrence and standard semen parameters (Bonduelle et al., 1998a).

It seems, therefore, that there is a slight, although significant, increase in the risk for de novo sex-chromosomal and structural aberrations after ICSI. However, there is a need for more information on this topic in order to define clearly the possible risks.

**Embryo freezing**

The incidence of congenital malformations in a group of 270 children born after replacement of cryopreserved embryos seems to be similar to that in a control group of spontaneously conceived babies (Wennerholm et al., 1997). This is also supported by the findings of Sutcliffe et al. (1995) in another smaller group of 91 children born after transfer of frozen-thawed embryos. Testart (1998) reported a 2.4% malformation rate in a cohort of children born after 15,567 transfers of frozen-thawed embryos in France, which is similar to the 2.8% malformation rate observed in a cohort of babies born after 93,015 fresh transfers. Therefore the cryopreservation process itself does not appear to have any impact on embryo health and subsequently on the rate of congenital anomaly.

**Child development**

Postnatal growth and health of children born after standard IVF and cryopreservation seem to be within the normal ranges. Wennerholm et al. (1991) followed-up 100 children born after conventional IVF for 18 months; these children had achieved heights and weights within the normal Swedish range. In another study by the same group, 264 infants conceived after transfer of frozen-thawed embryos and 261 infants conceived after standard IVF were compared with a control group of 252 spontaneously conceived children (Wennerholm et al., 1998). Postnatal growth was similar in these three groups. Another interesting observation from this study was that no increase in the incidence and degree of chronic illness as well as in the prevalence of common disease was observed in the cryopreserved and standard IVF groups as compared to the spontaneous control group (Wennerholm et al., 1998). Data from other studies evaluating the development of children conceived after standard IVF at 2 years of age (Saunders et al., 1996), between 12 and 45 months of age (Brandes et al., 1992) and between 6 and 13 years of age (Olivennes et al., 1997) are also reassuring in that they show normal growth.

The intelligence and the behaviour of children born after IVF was examined in an interesting study by Cederblad et al. (1996). In a child-psychiatric and neuropaediatric investigation of 99 children between 33 and 85 months of age, they found that their intellectual, emotional, somatic and social development was
Pregnancy and child outcome after assisted reproduction techniques

normal, although 28% of the children were born preterm and some of them had a complicated neonatal period.

Growth and development of ICSI children is another interesting field since ICSI is a more aggressive technique than standard IVF. In a recent study from Australia, Bowen et al. (1998) compared the medical and developmental outcome at 1 year of 89 children conceived by ICSI and 84 children conceived after standard IVF with a control group of 80 naturally conceived children. General health problems (hospital admissions, major health problems, visits to medical practitioners) and growth (weight, length and head circumference) were similar in the three groups. The developmental assessment was done using the Bayley scales (BSID II) for psychomotor (psychomotor development index – PDI) and mental (mental development index – MDI) development (Bayley, 1993). Although Bayley PDI scores at 1 year were similar in the three groups and most of the children conceived by ICSI had Bayley MDI scores within the normal range, as a group they scored significantly lower than the IVF and naturally conceived children, posing questions about the mental development of ICSI children.

However, these results should be interpreted with caution; the norms of BSID II were standardized only against a USA population and there may be doubts about its applicability to the Australian population, while the predictive value of BSID II for intellectual development at early school and later is unknown (te Velde et al., 1998). On the other hand, there were demographic differences in the parents between the three groups (occupation of fathers of ICSI children, mother’s education, country of origin and language spoken at home) which may also affect the results. Furthermore, Bonduelle et al. (1998b) followed up 201 ICSI and 131 IVF children prospectively at 2 years of age for their mental development, also carrying out Bayley tests, and the results of ICSI and IVF infants were compared to normal values for the Dutch general population. The overall results for ICSI and IVF children indicate similar scores to that of the general population. In multiple pregnancies, the results were somewhat lower than for singletons but there was no difference between ICSI and IVF multiples. The authors concluded that there is no indication for a slower mental development of ICSI infants compared to the general population (Bonduelle et al., 1998b).

Golombok et al. (1996) performed an interesting study examining family functioning in four different groups; families with a child conceived after IVF, with a child conceived after donor insemination, with a naturally conceived child and with an adopted child. The quality of parenting was superior in IVF and donor insemination families. Mothers were more emotionally involved with their child, mother-child and father-child interactions were superior, fathers contributed more to parenting and mothers reported less stress with parenting. Furthermore, children were found to have no differences for either the presence of psychological disorders or for their perception of the quality of family relationships.

Conclusions

It seems that pregnancies achieved after standard IVF bear an increased risk for prematurity and for low birth weight. Although this is mainly due to the higher
frequency of multiples, singleton IVF gestations seem also to have a higher risk compared with natural singleton conceptions. Increased maternal age, lower previous parity as well as the cause of infertility seem to be the most important causal factors. On the other hand, pregnancy outcome of singletons achieved after ICSI and after the transfer of cryopreserved embryos is similar to that of spontaneously conceived singletons, and pregnancy complications are related only to fetal multiplicity. A possible explanation is that women undergoing ICSI are usually healthy without any pelvic pathology. Moreover, parity is higher and stimulation is not needed in most of the transfers of frozen-thawed embryos. Pregnancies achieved after oocyte donation seem to carry a higher risk for complications, mainly due to the mother’s advanced age, and therefore oocyte donation should be avoided by women over 50 years old.

The incidence of congenital and chromosomal anomalies after standard IVF seems to be similar to that expected in the general population. It seems also that the incidence of congenital malformations is not increased after ICSI, although there is a need for more well designed studies on the basis of a common approach to detecting birth defects and using the same definitions. On the other hand, patients should be informed and counselled on the basis of the available data that there is a slightly higher risk for transmitted chromosomal aberrations of paternal origin and a higher risk of de novo, mainly sex-chromosomal aberrations. The possibility of transmitting fertility problems of genetic origin to the male offspring cannot also be excluded. Based on these data, a free choice of prenatal diagnosis should be available in all ICSI settings, according to some authors (Bonduelle et al., 1998a). The cryopreservation process seems to have no impact on the incidence of congenital and chromosomal anomalies.

Postnatal growth and development as well as the intelligence and behaviour of children born after standard IVF and embryo cryopreservation seem to be within the normal range. Growth of ICSI children is also normal while their mental development needs further investigation. Family functioning seems also to be better in families who have received assisted reproduction treatment.

References


B.C. Tarlatzis and G. Grimbizis


